UNIVERSITY OF GONDAR

COLLEGE OF MEDICINE AND HEALTH SCIENCES

SCHOOL OF BIOMEDICAL AND LABORATORY SCIENCES

DEPARTMENT OF MEDICAL MICROBIOLOGY

Assessment of bacterial pathogens, antimicrobial susceptibility pattern and associated risk factors among catheterized UTI suspected patients compared with non-catheterized patients at University of Gondar Referral Hospital, Northwest Ethiopia.

By: Wudu Tafere

Advisors: - Dr. Baye Gelaw (MSc, PhD, Asso.Proff)

- Mr. Teklay Gebrecherkos (BSc, MSc)

A thesis submitted to the Department of Medical Microbiology, School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar in partial fulfillment of the requirements for the degree of Masters of Science in Medical Microbiology.

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Gondar, Ethiopia

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CERTIFICATE

This is to certify that the thesis entitled **"Assessment of bacterial pathogens, antimicrobial susceptibility pattern and associated risk factors among catheterized UTI suspected patients compared with non-catheterized patients at University of Gondar Referral Hospital, Northwest Ethiopia.**" done by Wudu Tafere for the Masters of degree in Medical Microbiology was carried out under our supervision and the thesis has not been previously submitted in part or full for any degree or diploma in this or any other University.

Advisors	Sign	Date
1. Dr. Baye Gelaw	_____	15/06/2017
2. Mr. Teklay Gebrecherkos	_____	15/06/2017

June, 2017

Gondar, Ethiopia

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LIST OF ABBREVIATIONS

AMR: Anti Microbial Resistant

CAUTI: Catheter Associated Urinary Tract Infection

CFU: Colony Forming Unit

CLED: Cystine Lactose Electrolyte Deficient

ESBL: Extended Spectrum Beta Lactamase producer

HAI: Hospital Acquired Infection

HIV: Human Immunodeficiency Virus

ICU: Intensive Care Unit

MDR: Multi Drug Resistant

MRSA: Methicillin Resistance *Staphylococcus aureus*

SPSS: Statistical Package for Social Service

UTI: Urinary Tract Infection

WHO: World Health Organization

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ABSTRACT

Background: Urinary tract infections are among the most common bacterial infection frequently occur in community and hospital environment. Catheter associated urinary tract infection is a major health care problem responsible for an enormous aggregate burden of morbidity, mortality and increased health care costs. To date, little is known about the type of bacterial pathogens and their antimicrobial susceptibility pattern among catheterized and noncatheterized UTI patients, especially in the study area.

Objective: The aim of this study was to assess the bacterial pathogens, antimicrobial susceptibility pattern and associated risk factors among catheterized and non-catheterized UTI suspected patients at University of Gondar referral hospital.

Methods: A hospital based comparative cross sectional study was conducted from February to May/2017. A total of 208 (70=catheterized and 138=non-catheterized) clinically UTI suspected patients were recruited. After obtaining consent from each study subject, sociodemographic and clinical data were collected using pre tested structured questionnaire. Bacterial isolation from urine was done following standard bacteriological methods and antimicrobial susceptibility pattern was performed using Kirby-Bauer disk diffusion technique. Data was analyzed using SPSS version 20 computer software and p-value<0.05 was considered as statistically significant.

Results: The overall prevalence of culture confirmed UTI (catheterized = 41.4% and non-catheterized =17.4%) was 25.5% (95%CI=19.7 to 31.3%). The predominant bacterial isolate among catheterized and non-catheterized UTI patients was *Klebsiella pneumoniae* (21.9%) and *E. coli* (41.67%), respectively. Gram negative isolates were resistant to ampicillin and augmentin (100%) whereas, Gram positive isolates were resistant to cotrimoxazole (91%). Duration of catheter greater than 2 weeks (OR=18.00; 95%CI, 1.787-81.31) among catheterized patients, being female (OR=3.77; 95% CI, 1.30 - 10.1.97; p=0.015) and patients with underlying disease (OR=3.26; 95%CI, 1.15 - 9.27; p=0.027) in non-catheterized patients were significantly associated with UTI.

Conclusion: Catheterized patients for more than two weeks and non-catheterized females and patients with underlying diseases had significantly higher isolation rates of bacterial pathogens. Increasing resistance in pathogens isolated from catheterized UTI patients is frustrating. Rational use of antimicrobial agent should be thought of to prevent the emergence of multidrug resistance. Also, there is a need to establish standard guidelines on the care of catheter for all units in the hospital with a view to preventing nosocomial infections associated with the device in patients.

Key words: Urinary tract infection, catheter associated urinary tract infection, antimicrobial susceptibility**,** bacterial pathogens, North-west Ethiopia.

1. INTRODUCTION

1.1.Back ground

Urinary tract infections (UTIs) refer to infections occurring along the urinary tract from the perinephric fascia to the urethral meatus. It is the colonization, invasion and propagation of infectious agents in the urinary tract including upper and lower urinary tract (1, 2). Urinary tract infection is caused by the presence and growth of micro-organisms particularly bacterial pathogens within the genito-urinary tract system. It is one of the commonest disease mainly caused by bacterial pathogens in human worldwide(3).Infection may occur at any part of the genitourinary tract, including urethra, bladder, urethers, renal pelvis, or renal parenchyma(4).

The episode of UTI is classified as lower and upper urinary tract infection according to where it occurs: urethritis in urethra, cystitis in bladder, bacteriurias in urine, pyelonephritis in kidney and pyelitis in urethers (5). Most of these infections involve the lower urinary tract and could be either symptomatic or asymptomatic. Patients are said to have symptomatic urinary tract infections if there is significant bacteriuria ($\geq 10^5$cfu/ml) with sign and symptoms of acute UTI where as asymptomatic bacteriuria is the presence of significant bacteriuria without the symptoms of an acute urinary tract infection (6). The symptoms associated with UTIs include; dysuria (painful urination), polyuria (frequent urination), urinary urgency, haematuria, fever and flank pain. Infection in children less than one year may show additional symptoms like hypothermia, vomiting, bradycardia and lethargy (7). Most UTIs are caused by Gram-negative bacteria like *Escherichia coli, Klebsiella* spp, *Proteus mirabilis, Pseudomonas aeruginosa, Acinetobacter* spp and *Serratia* spp. and Gram-positive bacteria such as *Enterococcus* spp. and *Staphylococcus* spp (8). *Escherichia coli* and *Staphylococcus saprophyticus* cause approximately 80% and 15% of acute UTIs, respectively in patients without catheters (9).

Urinary tract infections have become the most common hospital acquired infections, accounting for as many as 35% of nosocomial infections, and they are the second most common cause of bacteremia in hospitalized patients (10).

Nosocomial urinary tract infection is usually associated with catheterization. The indwelling urinary catheter is an essential part of modern medical care and a variety of different

indwelling urinary catheters are used to monitor the various clinical parameters such as urinary tract obstructive lesions like benign prostatic hyperplasia who are awaiting surgery (11). Catheter associated urinary tract infection (CAUTI) can lead to such complications as prostatitis, epididymitis and orchitis in males, cystitis, pyelonephritis, bacteremia, endocarditis, septic arthritis and meningitis in patients (12). The risk of acquiring CAUTI depends on the method and duration of catheterization, the quality of catheter care and host susceptibility (13).

Women are three times greater risk for UTI than men because of short, straight anatomy of the urethra, and termination of female urethra beneath the labia resulting in colonization by colonic Gram-negative bacilli. Also UTIs are much more common in elderly than younger individuals due to immunity and frequently occur both in community and hospital environments (14).

The types of micro-organisms associated with CAUTIs have changed over time. Many infecting strains isolated from CAUTIs display markedly greater antimicrobial resistance than organisms that cause community-acquired UTIs. Catheter associated urinary tract infections are caused by a variety of resistant bacteria pathogens, including *Escherichia coli, Klebsiella* species, *Proteus* species, *Enterococci* species, *Pseudomonas* species, *Enterobacter* species *and Serratia* species. Many of these micro-organisms are part of the patients' endogenous bowel flora but they can also be acquired by cross contamination from hospital personnel or by exposure to non sterile equipments (15).

The emergence of antibiotic-resistant strains is a major therapeutic problem that is multifactorial and could be explained by several non exhaustive hypotheses. The influence of excessive and/or inappropriate antibiotic use, particularly of broad-spectrum agents prescribed empirically has been demonstrated (16). In vitro drug sensitivity testing in Ethiopia showed that both Gram negative and Gram-positive organisms were extremely resistant to ampicillin, amoxicillin, and tetracycline (17).

1.2. Statement of the problem

Urinary tract infection is one of the most common bacterial infections encountered in many parts of the world and associated with significant morbidity and mortality. It is estimated that 150 million cases of UTI occur on a global basis per year resulting in more than 4 billion pounds (6 billion dollars) in direct health care expenditure (18). Bacterial infections of the urinary tract have been reported in the community and the prevalence has been reported in all age groups and in both sexes (19, 20). Urinary tract infection is one of the most common infectious diseases, and reports showed that nearly 10% of people experience a UTI during their lifetime (21). It is estimated that 50-60% of all women after puberty experience at least one UTI episode during their lifetime and in 8% of UTI episodes the pathogens may stay silent (22).

Urinary tract infection is the fourth most common type of healthcare-associated infection, with an estimated 93,300 UTIs in acute care hospitals in 2011 and account for more than 12% of infections reported by acute care hospitals (23). Catheter acquired urinary tract infection is one of the most common health care acquired infection. 70% to 80% of these infections are attributable to the use of an indwelling urethral catheter. Recent prevalence surveys reported that urinary catheter is the most common indwelling device, with 17.5% of patients in 66 European hospitals having a catheter and 23.6% in 183 US hospitals. The daily risk of acquisition of urinary infection varies from 3% to 7% when an indwelling urinary catheter remains in place (24, 25).

Catheter associated urinary tract infections are associated with an excess mortality rate of 23 deaths per 1,000 inpatients and excess costs of $1,000/case, additional costs per hospital acquired infection (26). In 2007 the estimated deaths associated with HAIs in U.S. hospitals were 98,987: of these, 13,088 for urinary tract infections (27). According to WHO report of 2010 in USA, among the total Incidence of 5–6%; 1.7 million HAI affected patients, Urinary Tract Infection accounts 36%; 561,667 episodes and 13,088 deaths (28). A study in Greece Athens in 2010 also indicates the incidence of UTI was 7.7% and the incidence density was 4.09 cases/1000 urinary catheter-days. The mortality rate was also 22.8% among patients with CAUTI (29).

In Africa countries a study conducted in ICUs of Egypt in 2008 reported that among 757 patients with existing indwelling urinary catheters, a total of 161 episodes of infection were diagnosed, for an overall rate of 15.7 CAUTIs per 1000 catheter days (30). In Ethiopia, previous studies indicated high prevalence of hospital acquired infections. A rate of 15% and 26% for UTI were reported from Addis Ababa (31).

An estimated 17% to 69% of CAUTI may be preventable with implementation of evidence-based practices. This means that 380,000 infections and 9,000 deaths related to CAUTI per year could be prevented (32).The frequency of UTIs depends on many risk factors such as diabetes mellitus, advanced age, urinary tract obstructions, immune-suppression, and neurological disorders. Also urinary pathogens vary depending upon age, sex, catheterization, hospitalization and previous exposure of antimicrobials (33).

Antimicrobial drug resistance (AMR) among hospital and community acquired microorganisms is a problem both in developing and developed countries. Infections caused by resistant bacteria adversely affect treatment outcomes, treatment costs, disease spread and duration of illness, posing a serious challenge to the future of chemotherapy (34). Some of the economic effects of AMR have been attempted, and the findings are disturbing. Previous reports demonstrated that high incidence of antimicrobial resistance (68%) to the commonly prescribed antimicrobial agents was observed at Gondar. It was also previously reported that the isolated pathogens showed resistance from two to nine antimicrobials. The study documented that catheterized patients were 4.4 times at risk to develop UTI caused by drug resistant bacteria pathogens. Moreover, the report documented that nosocomial infections increased by 2.73 times the risk of UTIs (35).

Even though there are published information concerning the aetiology and susceptibility pattern of community acquired UTIs, data regarding CAUTIs in the study area is sparse. Thus, the aim of this study is to investigate the bacterial pathogens and their antimicrobial susceptibility patterns among UTI patients with history of catheter compared with non catheterised ones at University of Gondar referral hospital.

1.3.Literature review

The distributions of bacteria that cause UTIs are different in different parts of the world. Several studies have investigated pathogens of the UTIs and reported a steady increase in the level of resistance to commonly used antibiotics, including ampicillin and trimethoprim (36).

A prospective study conducted in Saudi Arabia in 2011 showed that the prevalence of community–acquired and hospital-acquired urinary tract infection was reported 55.3% and 44.7%, respectively. The majority of the bacteria were isolated from female (78.7%) patients but only 21.3% among males. *Escherichia coli* (48.1 and 43.2%) was the commonest cause of UTI in community and nosocomial settings followed by *Klebsiella* species (19.2%. *Escherichia coli* and *Klebsiella* species isolates were found to be resistant to ampicillin (75.4% and 90%, respectively). Moreover, *Klebsiella* species *(25%)* and *Proteus mirabilis* (19%) were less susceptible to nitrofurantoin (37).

Another study in Kashmir since 2012 documented higher proportions of female patients suffering from UTI (84.1%). *Escherichia coli* was the predominant isolate (53.8%) followed by *Klebsiella pneumoniae (*22.4%) and *Pseudomonas aeruginosa (*7.6%). The overall response to ampicillin by all isolates was less than 15% (38). One cross sectional study from Iran b/n 2009 to 2010 reported only 8.06% patients demonstrated positive urine cultures. In the same fashion, there were higher numbers of positive cases among females (88.69%) compared to males (11.3%). S*taphylococcus saprophyticus* isolates were the most frequent gram positive bacteria, exhibited high resistance to ampicillin, tetracycline and erythromycin (92.31%) and high susceptibility to nitrofurantoin and vancomycine (92.3%) (39).

Another cross sectional study conducted in eastern India in 2012 showed significant bacteriuria among 35.9% patients. The commonest organisms isolated were *E coli* (59.6%) followed by *Enterococcus* spp (14.9%) and *Klebsiella* species (10.6%). Among catheterized subjects apart from *E.coli* (64%), *Klebsiella* was found to be commoner (12%) than *Enterococcus* 10%. Most *Enterobactereacae* showed good response to nitrofurantoin and *Staphylococcus aureus* was responsive to vancomycin (40).

A study conducted among patients attended the Intensive Care Unit (ICU) of one Tertiary Care Hospital in India in 2014 reported that 20% of the demonstrated significant bacterial growth (>10^5 CFU/ml). The most common uropathogens isolated were *Escherichia coli* (40.0%) followed by *Staphylococcus aureus* (15.0%), *Pseudomonas aeruginosa (*5.0%) and *Enterococcus faecalis* (5.0%). Most of the Gram negative bacilli were sensitive to amikacin (75.0%) and nitrofurantoin (75.0%), while all Gram positive cocci were sensitive to vancomycin. MRSA was detected in 66.6% cases and 25.0% gram negative rods were ESBL producers (41).

In Africa, report from Nigeria in 2012 showed a 62.0% prevalence of bacterial uropathogens was isolated from symptomatic UTI patients. The dominant bacterial pathogen was *E. coli* (35.3%) followed by *Klebsiella* species (13.0%), *Proteus* species (4.0%), *P. aeruginosa* (2.0%) and *S. aureus* (8.0%). The antimicrobial susceptibility pattern of gram-negative bacteria showed low level of resistance (<60%) against ciprofloxacin, gentamicin and amoxicillin-clavulanic acid. However, there were high resistance (>80%) of *E. coli* to ampicillin and *Pseudomonas aeruginosa* to gentamicin (66.7%) (42).

In Benin, the prevalence of gram negative bacteria pathogens among catheterized patients presented with UTI was reported 79%. Similar to other study reports, *Escherichia coli* was found the dominant pathogen (63%) followed by *Pseudomonas* species (11%). The prevalence of *Staphylococcus aureus* was 21% (43). Among patients admitted to the critical care unit of a national hospital of Kenya due to urinary tract infections, the prevalence of *E.coli* was 23%. The proportion of *Klebsiella* species and *Enterococcus* species were 20% and 19% respectively. The report also documented that *E.coli* had high resistance to augmentin (65%), ceftriaxone (44%) and ampicillin (43%). *Klebsiella* species also demonstrated high level of resistance to augmentin (61.8%), gentamicin (47.4%) and cefotaxime (39.5%). High level of drug resistance was also observed on *Enterococcos* species which had a 58.3% resistance to ampicillin and 37.5% for gentamicin (44).

Different reports from different parts of Ethiopia demonstrated the burden of bacterial pathogens among patients suffering from UTI. Report from Jima University teaching hospital documented a 43.3% and 22.2% significant bacteriuria on catheterized and non catheterized UTI patients, respectively. The proportion of *Klebsiella* species was 33.3% followed by *E.*

coli (27.7%) and *Enterobacter* species (6%). Gram-negative bacteria isolated in both groups showed a high level of resistance (88-100%) to ampicillin and low level of resistance (16-24%) observed to amikacin, ciprofloxacin, nalidxic acid and nitrofurantoin (45).

A retrospective study conducted in Addis Ababa demonstrated an overall prevalence of urinary tract infection of 23.32 % and the highest prevalence was obtained among age groups 21-30 years (27.16%). The bacterial pathogens isolated were *Escherichia coli* (44.62%) followed by *Klebsella* species *(*16.81%), Coagulase negative *Staphylococci* species (6.06%) and *Enterococci* species (5.06%).In vitro drug sensitivity testing showed that both gram negative and gram-positive organisms were extremely resistant to ampicillin (83.93%), amoxicillin (78.87%) and tetracycline (77.75%) (46). A prospective study in Mekelle since 2007 showed that among 96 catheterized patients, 38/96 (39.5%) developed nosocomial UTI where as 12 patients out of the 96 who were catheterized (12.5%) developed community-acquired UTI (47).

Bacterial pathogens among UTI patients were analyzed using retrospective data at Dessie since 2012. The proportion of *E. coli*, *Pseudomonas* species, *Proteus* species, *S. aureus* and *Klebsiella* species were 60.29%, 8.68%, 7.79%, 7.35% and 5.88%, respectively. *E.coli* is almost resistant to Ampicillin and tetracycline. Similarly *Pseudomonas* and *proteus* species were resistant to almost all antibiotics except gentamycin (48). On the other hand a prospective study in Dessie at different point in time showed an overall significant bacteriuria of 22.7%. *Escherichia coli* were the dominant isolate (63.6%) followed by *Klebsiella* species *(*8.5*%)* and *Proteus* species (8.2%). The three most frequently isolated bacteria had resistance rates of 80.1% - 90% to amoxicillin and tetracycline and sensitivity rates of 0 to 25% to nitrofurantoin, ciprofloxacin and gentamicin (49).

Another study conducted in Bahir Dar by the year 2010 indicates that out of 1254 patients, 118 (9.4%) developed nosocomial UTIs. *E. coli, S.aureus* and *K. pneumoniae* were the most predominant isolates. Most bacterial isolates showed high resistance rates (>80%) to ampicillin and amoxicillin/clavulanic acid (50). Previous report (2008) from the same area showed that from 529 urine specimens, bacterial isolates were found in 160 (30.2%). Of these, 116 (72.5%) of the isolates were gram negatives. The overall multiple drug resistance was 93.1% and 4.4% were sensitive to all antibiotics tested (51).

1.4. Significance of the study

A urinary tract infection is an infection involving any part of the urinary system, including urethra, bladder, ureter and kidney (4). UTIs are the most common type of health care-associated infection. Among UTIs acquired in hospitals, approximately 70 to 80 % are associated with a urinary catheter, which is a tube inserted into the bladder through the urethra to drain urine (25). Catheterization is a frequent procedure performed for patients with urinary tract obstructive lesions such as benign prostatic hyperplasia who are awaiting surgery and also as a routine in the management of unconscious patients to monitor their urine output (11). The most important risk factor for developing a catheter-associated UTI is prolonged use of the urinary catheter (13).

This study provides information about the burden of bacterial pathogens, antimicrobial susceptibility pattern and associated risk factors among UTI suspected patients who used catheters compared with non-catheterized once. Even though there are published information concerning the aetiology and susceptibility pattern of community acquired and hospital acquired UTIs, local data regarding CAUTIs are sparse at University of Gondar referral hospital in particular and other parts of Ethiopia in general. Therefore, the present study investigates the bacterial pathogens and their antimicrobial susceptibility pattern among UTI patients with history of catheter compared with non-catheterized ones at University of Gondar referral hospital. This also provides evidences for the level of control and calls for concerted efforts at all levels including regulatory bodies and the public healthcare providers for better management of catheter associated UTIs. This study is also important for clinician in order to facilitate the empiric treatment of UTI patients where culture and drug susceptibility test is impossible. In addition to these, it also used as base line data to conduct further studies.

2. OBJECTIVES

2.1. General objective

- The overall aim of this study was to assess the bacterial pathogens, their antimicrobial susceptibility pattern and associated risk factors among catheterized UTI suspected patients compared with non-catheterized ones.

2.2. Specific objectives

⇒To identify bacterial pathogens among UTI patients.

⇒To compare the prevalence of bacterial pathogens between catheterized and non-catheterized UTI patients.

⇒To determine the drug susceptibility patterns of bacterial pathogens isolated from UTI patients.

⇒To compare the drug susceptibility pattern of bacterial pathogens isolated from catheterized versus non-catheterized UTI patients.

⇒To identify risk factors associated with UTIs.

3. MATERIALS AND METHODS

3.1. Study area

The study was conducted in University of Gondar referral Hospital located in Gondar town which is located 747 km from the capital city of the country, Addis Ababa and 182 km far from Bahir Dar which is the capital city of the Amhara regional state. According to the recent administration, the town has 12 sub cities which consist of 21 kebeles. Gondar is one of the ancient and densely populated towns in Ethiopia. Its astronomical location is 12°45′ north latitude and 37°45′ east longitudes with an elevation of 2,160 meters above sea level. According to the 2007 population and housing census result of Ethiopia, the town had total population of 206,987 (98,085 males and 108,902 females). In Gondar town there is one referral hospital, 8 health centres, and 15 private clinics serving the population. University of Gondar referral Hospital is the only referral hospital in the town which serves for 5 million population with 1000 beds and different wards. The hospital consists of an operating room, intensive care unit (ICU), fistula center, 13 different wards and outpatient departments.

3.2. Study design and period

A Hospital based comparative cross-sectional prospective study was conducted from February to May, 2017 at University of Gondar referral hospital.

3.3. Population

3.3.1. Source population

The source population were all patients seeking health service at University of Gondar referral hospital during the study period.

3.3.2. Study population

The study population were all patients suspected of UTI irrespective of catheter use seeking health service at University of Gondar referral hospital with in the study period.

3.4. Inclusion and exclusion criteria

3.4.1. Inclusion criteria

All patients with sign and symptoms of UTIs seeking health service at the University of Gondar referral hospital and who are volunteer to participate was included in the study.

3.4.2. Exclusion criteria

Patients with UTIs but treated with antimicrobials within the previous 14 days, those patients catheterized for less than 48 hours during the specimen collection time and catheterized patients with symptoms of UTI before catheterization were excluded from this study.

3.5. Study Variables

3.5.1. Dependent variable

- The prevalence of bacterial pathogens and their antimicrobial susceptibility pattern.

3.5.2. Independent variables

Age, sex, residence, marital status, occupation, patient setting, pregnancy, history of previous UTI, history of previous catheterization, duration of catheterization, history of underlying disease such as HIV and diabetics.

3.6.Sample size determination and sampling technique

3.6.1. Sample size

Sample size was determined by using EPI version-7 statistical soft ware package where P1 (prevalence of UTI among catheterized study subjects) found 43.3%, P2 (prevalence of UTI in non catheterized study subjects) found 22.2 % (45). At 95% confidence interval and power of test being 80%, n1 (number of catheterized study subjects), n2 (number of non-catheterized study subjects) =1: 2

Then n_{1i} =63 and n_{2i} =126, Ni =63+126 = 189

By considering a 10% non response rate N_F = Ni+10% of Ni =189+19 =208 (N1f =70 & N2f =138)

3.6.2. Sampling technique

Patients with symptoms of UTIs were consecutively recruited by convenient sampling technique and included in the study until the required sample size was obtained for each category.

3.7.Definition of terms

Catheter associated urinary tract infection (CAUTI): is a type of infection resulted up on the use of indwelling urinary catheter is in place for >2 calendar days on the date of event.

Indwelling catheter: A drainage tube that is inserted into the urinary bladder through the urethra, is left in place, and is connected to a drainage bag.

Non-CAUTI: Patient did not have a urinary catheter in place on the date of event nor the day before the date of UTI.

Mid-stream urine specimen: a specimen obtained from the middle part of urine flow.
Multidrug resistance (MDR): It is defined as non-susceptibility to at least one agent in three or more antimicrobial categories.

Underlying disease: a disease that cause another issue or disease

3.8. Data collection

3.8.1. Socio demographic and clinical data collection

After taking written informed consent, socio-demographic characteristics, clinical data and associated risk factors were collected by trained nurse using pretested structured and standardized questionnaire guided interview.

3.8.2. Urine sample collection

A freshly voided clean catch midstream urine samples (10-20 ml) was collected from non catheterized UTI suspected patients in a wide mouth sterile container with screw cap tops after cleansing the genitals with soap and water. Catheter urine specimens (10-20ml) from catheterized patients was also collected from the distal edge of the catheter tube (after cleaning with an antiseptic) using a sterile needle and syringe into sterile urine container. The

urine specimens were then delivered to teaching microbiology laboratory immediately and processed within two hour.

3.8.3. Sample processing

A. **Culture and identification**

Urine specimens obtained from both groups were inoculated on CLED media using calibrated loop (0.001ml). Cultures were incubated in aerobic atmosphere at 37ºC for 24 hours. The growth of bacterial pathogens was inspected visually and graded for the presence of significant bacteriuria. A significant bacteriuria is defined as colony count $\geq 10^5$ cfu/ml for mid stream urine and $\geq 10^2$ cfu/ml for catheter urine sample obtained from catheterized patients. Inoculated culture media demonstrated as a significant bacteriuria was sub-cultured on Blood agar plate and MacConkey agar plate and incubated for further 24 hours.

All positive cultures were further identified by their colony characteristics appearance on the media, Gram-staining reaction and confirmed by the pattern of biochemical reactions using standard procedures. Gram negative bacteria were identified by indole production, H_2S production in TSI/KIA agar, citrate utilization, motility test, urease test, oxidase, carbohydrate utilization test, gas production, sugar fermentation and others. For gram positive bacteria coagulase test, novobiacin test, catalase other tests were used for species identification (52).

B. **Antimicrobial susceptibility testing**

Antimicrobial susceptibility testing was carried out on each identified organism by Kery bauer disc diffusion method on Muller Hinton agar (MHA). After a pure culture was obtained, a loop full of bacteria was taken from a colony and was transferred to a tube containing 5ml sterile normal saline (0.85% NaCl) and mixed gently until it formed a homogenous suspension. The turbidity of the suspension was determined in comparison with 0.5 McFarland standards. A sterile swab was dipped in to the suspension and excess suspension was removed by pressing the swab against the wall of the tube. The swab was used to distribute the bacteria suspension evenly over the entire surface of MHA. The inoculated plates were left at room temperature for 3-5 minutes until it dry. The antimicrobial impregnated disks were placed with sterile forceps on the agar surface at least 24mm away from each other to avoid the overlapping zone of inhibition. After placing the

disk the plate was allowed to stand for 30 minutes to dissolve the antibiotic in the media. Then, the plates were inverted and incubated at 37∘C for 18-24 hrs and were read for the diameter of zone of inhibition by using a ruler.

Grades of susceptibility pattern were recognized as sensitive, intermediate, and resistant by comparison of zone of inhibition as indicated in the manufacturer's guide. Intermediate results were few in number and therefore were considered as resistant for convenience.

The antimicrobial agents tested were obtained from Oxoid (UK) in the following concentrations: Amikacin (30 µg), Ampicillin (10µg), Amoxicillin-clavulanic acid (20/10 µg), Ceftriaxone (30 µg), Ciprofloxacin (5 µg), Nitrofurantoin (30 µg), Nalidixic acid (30 µg, Cefepime (30 µg), Cefexime (5 µg), Piperacillin (100 µg), Ceftazidime (30 µg), Gentamycin (10 µg) and Norfloxacin (5 µg) for Gram negative bacteria. Whereas, Erythromycin (10 µg), Penicillin (30 µg), Tetracycline (30 µg), Vancomycine (30 µg), Cotrimoxazole (75 µg) and Cefoxitine (30 µg), Nitrofurantoin (300 µg) and Norfloxacin (10%) were for gram positive bacteria. The results were interpreted according to the most recent version of the National Committee for Clinical Laboratory Standards (NCCLS, 2017) (52, 53).

3.9. Quality control

The reliability of the study findings was guaranteed by implementing Quality Control (QC) measures throughout the whole process of the laboratory work. All materials, equipment, reagents and procedures were adequately controlled. Pre-analytical, analytical and post-analytical stages of quality assurance and Standard Operating Procedures (SOPs) were strictly followed. Pre-tested structured questionnaire guided interview was used for data collection on socio-demographic characteristics, clinical data and associated risk factors. The validity and completeness of the questionnaire was daily checked by the principal investigator.

Sterility of culture media was checked by incubating 5% of the batch at 35-37^{O}C overnight and was evaluated for possible contamination. The standard reference bacteria strains such as *S aureus* (ATCC25923) *P. aeruginosa* (ATCC-27853) and *E. coli* (ATCC-25922) was tested weekly as controls on the biochemical tests and agar plates including Mueller Hinton agar with antimicrobial discs to assure testing performance of the potency of antimicrobial discs. To standardize the inoculums density of bacterial suspension for the susceptibility test, 0.5

McFarland standard was used (52, 53). More over the whole procedure and result interpretation were cross checked by senior laboratory professionals.

3.10. Data analysis

Data were checked for completeness, cleaned manually, entered and analyzed using SPSS version 20 computer software. Frequencies and cross tabulations were used to summarize descriptive statistics. Odd ratio and adjusted odds ratio at 95% confidence interval were used to interpret the strength of association. Chi-square test, bivariate and multivariate logistic regressions were employed to assess the association between outcome and explanatory variables. p-values < 0.05 were considered statistically significant.

3.11. Ethical considerations

Ethical clearance was obtained from University of Gondar, School of biomedical and laboratory sciences ethical review committee and official letter of co-operations were provided to Gondar referral hospital prior to data collection. Written informed consent/assent was obtained from study participants, guardians or caretakers of children after explaining the purpose and objective of the study. Any patient who is not willing to participate in the study would not be forced to participate. They were informed that all data and sample obtained from them was kept confidential by using codes instead of any personal identifiers and is meant only for the purpose of the study. The laboratory results from the study participant were communicated to their physicians for appropriate treatment.

4. RESULTS

4.1. Socio-demographic characteristics of study participants

A total of 208 study subjects (70 catheterized and 138 noncatheterized) patients suspected of UTI were included in the study. The mean (SD) age of catheterized and non-catheterized UTI patients were 54.6 ± 21.7 years and 35.9 ± 15.1 years, respectively (range from 10 to 95 years and 10 to 80 years, respectively). There was male preponderance 39 (55.7%) in catheterized UTI patients as compared to non-catheterized patients where the majority 76 (55.1%) were females. Among the study participants, 109 (52%) lived in rural areas, of whom 94 (45%) were farmers. Data on the educational and marital status also demonstrated that 100(48%) were unable to write and read and 136(66%) were married (Table1).

4.2. Major clinical features observed among UTI patients

Among the presenting clinical features for catheterized UTI suspected patients, fever, flank pain and suprapubic pain were reported in 46(65.7%), 44(62.9%), and 39(55.7%) respectively. Tenderness and dysuria were also reported in 36(51.4%) and 18(25.7%) respectively whereas in noncatheterized UTI suspected patients, flank pain 96(69.5%), suprapubic pain 89(64.5%), frequency 76(55%) and fever 64(46.4%) were complained by study subjects. Moreover, dysuria 46 (33.3%), tenderness 35 (25.4%) and urgency 4(2.9%) were also reported (Table-2).

Culture positivity of urine culture was much higher for catheterized UTI suspected patients who presented with dysuria (AOR=13.42, 95% CI= 2.771-65.072) and flank pain (AOR=6.895, 95% CI= 1.613-29.481). On the other hand, urine culture among non-catheterized UTI suspected patients had higher odds of culture positivity among patients presented with dysuria (AOR=3.45, 95%CI=1.214-9.786), suprapubic pain (AOR=4.78, CI=1.354-16.864) and tenderness (AOR=7.00, CI=2.436-20.093) as compared to their counterparts.

4.3. Prevalence of significant bacteriuria among catheterized and non-catheterized patients

Culture result of the present study showed that a total of 53 patients (25.5%) (95%CI=19.7-31.3) suspected for UTI demonstrated significant bacteriuria. Significantly, higher prevalence of significant bacteriuria was observed among catheterized patients 29/70 (41.43%) compared with non-catheterized cases 24/138 (17.40 %) ($p<0.05$). The occurrence of significant bacteriuria among catheterized UTI suspected patients were 3 times more likely [AOR=3.36, 95% CI= (1.75, 6.42)] as compared to non catheterized suspected patients (Table 3).

Table 1: Socio demographic characteristics of catheterized and non-catheterized UTI patients at University of Gondar Referral Hospital, February to May/2017.

Characteristics	Catheterization status		
	Catheterized n (%)	Non-catheterized n (%)	Total n (%)
Sex			
Male	39 (55.7)	62 (44.9)	93 (45)
Female	31 (44.3)	76 (55.1)	115 (55)
Total	70 (100)	138 (100)	208 (100)
Age			
<15	2 (2.9)	3 (2.2)	5 (2.4)
15-24	3 (4.3)	27 (19.6)	30 (14.4)
25-34	11(15.7)	50 (36.2)	61 (29.40
35-45	11(15.7)	25 (18.1)	36 (17.3)
>45	43 (61.4)	33 (23.9)	76 (36.5)
Total	70 (100)	138 (100)	208 (100)
Residence			
Rural	44 (62.9)	65 (47.1)	109 (52)
Urban	26 (37.1)	73 (52.9)	99 (48)
Total	70 (100)	138 (100)	208 (100)
Marital status			
Married	43 (61.4)	93 (67.4)	136 (66)
Single	5 (7.1)	24 (17.4)	29 (14)
Divorced	5 (7.1)	6 (4.3)	11 (5)
Widowed	17 (24.3)	15 (10.9)	32 (15)
Total No (%)	70 (100)	138 (100)	208 (100)
Educational status			
Unable to write and read	41(58.6)	59 (42.8)	100 (48)
Read and write only	10 (14.3)	10 (7.2)	20 (10)
Primary	8 (11.4)	22 (15.9)	30 (14)
Secondary	8 (11.4)	30 (21.7)	38 (18)
College and above	3 (4.3)	17 (12.3)	20 (10)
Total No (%)	70 (100)	138 (100)	208 (100)
Occupation			
Civil servant	5 (7.1)	23 (16.7)	28 (13.5)
Merchant	9 (12.9)	20 (14.5)	29 (14)
Farmer	39 (55.7)	55 (39.9)	94 (45)
Housewife	9 (12.9)	17 (12.3)	26 (12.5)
Self employer	4 (5.7)	9 (6.5)	13 (6.3)
Student	4 (5.7)	14 (10.1)	18 (8.7)
Total No (%)	70 (100)	138 (100)	208 (100)
Patient setting			
Outpatient	0(0)	128 (92.8)	128 (61.5)
Inpatient	70 (100)	10 (7.2)	80 (38.5)
Total No (%)	70 (100)	138 (100)	208 (100)

Table 2: Association of clinical features with UTI among catheterized and non-catheterized patients at University of Gondar Referral Hospital, February to May/2017.

		Catheterized patients					Non-catheterized patients				
		Significant Bacteriuria					Significant Bacteriuria				
clinical features		Pos n (%)	Neg n (%)	COR	AOR (95%CI)	P-value	Pos n(%)	Neg n(%)	COR	AOR (95%CI)	P-value
Fever	No	11 (45.8)	13 (54.2)	1			9 (12.2)	65 (87.8)	1	1	
	Yes	18 (39.1)	28 (60.9)	0.760			15 (23.4)	49 (76.6)	2.211*	2.616 (0.948-7.217)	0.63
Dysuria	No	16 (30.8)	36 (69.2)	1	1		12 (13)	80 (87)	1	1	
	Yes	13 (72.2)	5 (27.8)	5.850*	13.427 (2.771-65.072)	0.001*	12 (26.1)	34 (73.9)	2.353*	3.446 (1.214-9.786)	0.020*
Flank pain	No	8 (30.8)	18 (69.2)	1	1		2 (6.2)	30 (93.8)	1	1	
	Yes	21 (47.7)	23 (52.3)	2.054*	6.895 (1.613-29.481)	0.009*	22 (20.8)	84 (79.2)	1.357		
Suprapubic pain	No	9 (29)	22 (71)	1	1		4 (8.2)	45 (91.8)	1	1	
	Yes	20 (51.3)	19 (48.7)	2.573*	3.225 (0.967-10.755)	0.057	20 (22.5)	69 (87.5)	3.261*	4.778(1.354-16.864)	0.015*
Tenderness	No	10 (29.4)	24 (70.6)	1	1		9 (8.7)	94 (91.3)	1	1	
	Yes	19 (57.8)	17 (42.2)	2.682*	2.914 (0.892-9.517)	0.077	15 (42.9)	20 (57.1)	5.555*	6.997(2.436-20.093)	0.000*

Table 3: Comparison of the prevalence of significant bacteriuria among catheterized and non-catheterized patients at University of Gondar Referral Hospital, February to May/2017.

Catheterization status	Presence of significant bacteriuria					
	Positive n (%)	**Negative n (%)**	**Total n (%)**	**OR**	**95%CI**	**P-value**
catheterized	29 (41.43)	41 (58.57)	70(33.7)	3.360	1.753-6.423	0.000
Non-catheterized	24 (17.40)	114 (82.60)	138 (66.3)	1	-	-
Total No (%)	53(25.48)	155(74.42)	208(100)			

4.4. Prevalence of uropathogenic bacterial isolates

A total of 56 different types of bacterial pathogens were identified among patients suspected for UTI. Of these, 25/56 (45%) were from non-catheterized and 31/56 (55%) from catheterized UTI patients respectively. More than one bacteria (mixed type) were isolated in both noncatheterized and catheterized groups in the proportions of 1/24(4%) and 2/29(7%) respectively. Gram negative bacteria were commonly isolated, 32 (57%) than the Gram positive bacterial spps 24 (43%). *E. coli* 12/56(21.4%) was the most commonly isolated bacteria among UTI suspected patients irrespective of catheter use followed by Coagulase negative *staphylococcus* spp 11(19.6%), *Klebsiella pneumoniae* 9 (16.1%), *S.aureus* 9(16.1%), *Enterococcus* spp 4(7.1%) and *Serratia* spp 3(35.4%).

The most frequently isolated bacterial species from non-catheterized patients was *E.coli* 10 (40%) followed by Coagulase negative *staphylococcus* spp which accounts 6(24%). Among catheterized patients, *Klebsiella pneumoniae* and *S.aureus* were found to be the most frequently isolated pathogens 7(22.6%) and 6(19.4%), respectively. Among the bacterial isolate, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Enterobacter* species and *Citrobacter* species were isolated only from catheterized patients. Isolation of *E. coli* was significantly more frequent in non-catheterized (10/12, 83.3 %) than in catheterized (2/12, 16.7%) (X^2= 9.3, p-value=0.002). On the other hand, all 1(100%) of *Proteus mirabilis*, 2(100%) *Pseudomonas aeruginosa*, 3(100%) *Enterobacter* species and 2 (100%) *Citrobacter* species; and the majority (7/9, 77.8%) of *Klebsiella pneumoniae and S.aureus* (6/9, 66.7%), though statistically insignificant, were isolated from catheterized patients (Table 4).

Table 4: The proportion of Gram negative and Gram negative bacterial pathogens among catheterized and non-catheterized UTI patients at University of Gondar Referral Hospital, February to May/2017.

Bacterial isolate	Catheterization status				
	Catheterized No (%)	Non catheterized No (%)	Total No (%)	X^2	P-value
E.coli	2 (16.7)	10 (83.3)	12 (21.4)	9.251	0.002*
K.pneumonia	7 (77.8)	2 (22.2)	9 (16)	2.181	0.140
P.aeruginosa	2 (100)	0 (0)	2 (3.6)	1.673	0.196
P.mirabilis	1 (100)	0 (0)	1 (1.8)	0.821	0.365
Enterobacter spps	3 (100)	0 (0)	3 (5.4)	2.556	0.110
Citrobacter spps	2 (100)	0 (0)	2 (3.6)	1.673	0.196
Serratia spps	1 (33.3)	2 (66.7)	3 (5.4)	0.622	0.430
S.aureus	6 (66.7)	3 (33.3)	9 (16.1)	0.555	0.456
Enterococcus spps	2 (50)	2 (50)	4 (7.1)	0.50	0.823
CONS	5 (45.5)	6 (54.5)	11 (19.6)	0.543	0.461
Total No (%)	**31 (100)**	**25 (100)**	**56 (100)**		

4.5. Association of risk factors with bacteria caused UTI

In this study sex, age, duration of the application of catheter, previous history of UTI, previous history of catheterization, history of underlying diseases, pregnancy and patient setting were used as potential risk factors for UTI. Among catheterized patients, multivariate regression analysis showed no statistically significant association between the risk factors and CAUTI except the duration of application of catheter.

Data showed that catheterized patients who had duration of catheterization >2 weeks were about 18 times [p=0.014, AOR=18.00, 95%CI= (1.787-81.31)] more likely to develop UTI than those who had duration of catheterization with 3days. Even though statistically insignificant, a bivariate analysis showed that risk of developing CAUTI in males were 1.9 times (OR=1.995; 95%CI: 0.748-5.318), higher than females. Moreover, as the duration of catheterization increased the risk of developing CAUTI increased: patients catheterized for 1 week were 2.1 times (OR=2.100; 95%CI; 0.666-6.625) and for 2 weeks were 4.5 times (OR=4.500; 95%CI; 0.601-33.708) more likely to develop CAUTI, respectively as compared to those patients catheterized for three days.

In the case of non-catheterized patients sex was significantly associated with the prevalence of UTI. The prevalence of UTI in noncatheterized female patients (25%) was higher than in male patients (8.1%). The probabilities of being a female in non catheterized patients were 4 times higher to develop UTI as compared to males. [AOR=3.77, 95% CI= (1.30-10.1.97), p=0.015]. The current study also showed statistically significant association between UTI and that of underlying disease among non-catheterized patients. Moreover, patients that have history of underlying disease were 3 times at higher risk to develop UTI (AOR=3.262; 95% CI= (1.147-9.273); P=0.027) (Table 5).

Table 5: Association of risk factors with UTI among catheterized and non-catheterized patients at University of Gondar Referral Hospital,February to May/2017.

	Catheterized patients					Non-catheterized patients				
Variables	**Significant Bacteriuria**					**Significant Bacteriuria**				
	Pos n (%)	Neg n (%)	COR	AOR (95%CI)	P-value	Pos n(%)	Neg n(%)	COR	AOR (95%CI)	P-value
Sex Male	19 (48.7)	20 (51.3)	1	1		5 (8.1)	57 (91.9)	1	1	
Female	10 (32.3)	21 (67.7)	1.995*	2.213 (0.755-6.481)	0.147	19 (25)	57 (75)	3.800*	3.770(1.29510.971)	0.015*
Age (Years)										
<15	1 (50)	1 (50)	1	1		1 (33.3)	2 (67.7)	1	1	
15-24	2 (67.7)	1 (33.3)	2.000			3 (11.1)	24 (88.9)	0.250		
25-34	4 (36.4)	7 (63.6)	0.571			6 (12)	44 (88)	0.273		
35-45	4 (36.4)	7 (63.6)	0.571			5 (20)	20 (80)	0.500		
>45	18 (41.9)	25 (58.1)	0.720			9 (27.3)	24 (72.7)	0.750		
Catheter duration										
3 days	6 (25)	18 (75)	1	1						
1 week	14 (41.2)	20 (58.8)	2.100*	2.100 (0.666-6.625)	0.206					
2 weeks	3 (60)	2 (40)	4.500*	4.500 (0.601-33.708)	0.143					
>2 weeks	6 (85.7)	1 (14.3)	18.00*	18.00(1.787-81.311)	0.014*					
Previous catheterization										
No	28 (42.4)	38 (57.6)	1	1		23 (17)	112 (83)	1	1	
Yes	1 (25)	3 (75)	0.452			1(33.3)	2 (66.7)	2.435		
Previous UTI										
No	28 (41.2)	40 (58.8)	1	1		17 (16.2)	88 (83.8)	1	1	
Yes	1 (50)	1 (50)	1.429			7 (21.2)	25 (78.8)	1.394		
Underlying disease										
No	23 (42.6)	31 (57.4)	1	1		16 (13.9)	99 (86.1)	1	1	
Yes	6 (37.5)	10 (62.5)	0.809			8 (34.8)	15 (65.2)	3.300*	3.262 (1.147-9.273)	0.027*

4.6. Antimicrobial susceptibility patterns of bacterial isolates

The antimicrobial susceptibility patterns of the Gram negative and Gram positive bacterial isolates are presented in (Table 6 and 7) respectively. All Gram-negative isolates from both groups of patients (non-catheterized and catheterized) showed a high level (100 %) of resistance to ampicillin and augmentin. *E.coli* isolate showed high level of resistance to augmentin and ampicillin (n=12; 100%) and nalidixic acid (n=5; 41.66 %%). On the other hand high level of sensitivity were found to nitrofurantoin, gentamicin, amikacin and ceftriaxone each 11 (91.7%) and cefepime 10(83.4%). *K.pneumoniae* also showed high level of resistance to augmentin and ampicillin (n=9; 100%) but 88.9% (n=8) isolates were sensitive to ciprofloxacin, norfloxacin and cefepime. *Proteus mirabilis*, *Enterobacter* species and *Citrobacter* species which were isolated only catheterized patients showed high level of resistance to many antimicrobial disks. *Proteus mirabilis* showed high level of resistance to 10 antimicrobials (100%) but it was susceptible for amikacin. *Enterobacter* spp and *Citrobacter* spp were also 100% resistant to ceftriaxone, amikacin, augmentin, ampicillin and cefepime. However, *Enterobacter* spp were sensitive 2 (100%) to nitrofurantoin and amikacin. On the other all *pseudomonas aeruginosa* which was also isolated only catheterized patients showed 2(100%) sensitivity for all antimicrobials tested (Table 6).

The antimicrobial susceptibility pattern of the Gram positive bacterial isolate showed that coagulase negative *Staphylococcus* species were highly resistant to cotrimoxazole (n=9; 82%), ciprofloxacin and cefoxitine each (n=6; 55%), and tetracycline (n=5; 45%). However, coagulase negative S*taphylococcus* species isolates were sensitive to nitrofurantoin (n=11; 100%) and norfloxacin (n=8; 73%). The majority of the *S.aureus* were resistant to Cotrimoxazole (n=8; 89 %), penicillin and tetracycline each (n=7; 78%) and cefoxitine (n=5; 57%). Nevertheless, most isolates of *S.aureus* were sensitive to nitrofurantoin (n=9; 100%), ciprofloxacin (n=7; 78%), and norfloxacin (n=6; 67%). Since 5(57%) of *S.aureus* isolates were resistance to cefoxitine, methicillin resistance *S.aureus* was detected in 55.6% cases.
On the other hand, all *Enterococcus* species were 4 (100%) resistant to tetracycline, erythromycin and ciprofloxacin. Among all isolates of *Enterococcus* species, 50% were vancomycine resistant.

4.6.1. Comparison of antimicrobial resistance patterns of isolates from catheterized and noncatheterized UTI patients

E.coli pathogens isolated from catheterized patients showed high level of resistance to ampicillin and augmentin (100%) and 50% of the isolates also showed resistance to ciprofloxacin, norfloxacin, nalidixic acid, cefepime and cefexime whereas, 100% of *E.coli* isolates from non-catheterized patients were also resistant to augmentin and ampicillin. In addition, relatively lower resistance to ciprofloxacin, norfloxacin, nalidixic acid, cefepime and cefexime (20%, 20%, 40%, 20, 10%, respectively) was observed among non-catheterized patients (Table 6).

Coagulase negative *Staphylococci* isolated from catheterized patients showed high level of resistant to cefoxitine and ciprofloxacin (100% and 60%, respectively). However, it showed low level of resistance to cefoxitine (17%) and ciprofloxacin (50%) for noncatheterized patients. *S.aureus* isolate from catheterized patients also showed high level of resistance to penicillin, cotrimoxazole, tetracycline, gentamycin and cefoxitine (100%, 100%, 80%, 67% respectively) whereas, isolates from noncatheterized patients showed low level of resistance for cotrimoxazole, tetracycline and penicillin (67%, 67%, 33%, respectively).

The overall prevalence of multidrug resistance pattern was 41 (73.2%) while only 3(5.4%) isolates were susceptible to all antimicrobial disks. Of the 9 (16.1%) *K. pneumoniae* isolates, 8(88.9%) isolates showed multiple drug resistance and only one was found to be resistant to one antibiotic. On the other hand, all isolates of *Enterococcus* spps, *Citrobacter* spps, *Enterobacter* spps and *Proteus mirabilis* showed multidrug resistance to three or more antibiotic classes (Table 8).

Table 6: Antimicrobial sensitivity pattern of Gram negative bacteria isolated from catheterized and non-catheterized UTI patients at University of Gondar Referral Hospital, February to May/2017.

Catheterized case	DSP	Antimicrobial agent number (%)												
		CPR	CTR	NOR	NIT	NAL	AUG	AMP	CXM	CFP	CN	AKN	CAZ	PRL
***E.coli* (n=2)**	S	1(50)	1(100)	1(50)	2(100)	1(50)	0(0)	0(0)	1(50)	1(50)	2(100)	2(100)	-	-
	R	1(50)	0(0)	1(50)	0(0)	1(50)	2(100)	2(100)	1(50)	1(50)	0	0(0)	-	-
***K.pneumoniae* (n=7)**	S	6(86)	4(57)	6(86)	5(71)	6(86)	0(0)	0(0)	5(71)	6(86)	4(57)	5(71)	-	-
	R	1(14)	3(43)	1(14)	2(29)	1(14)	7(100)	7(100)	2(29)	1(14)	3(43)	2(29)	-	-
***Enterobacter* spp(n=3)**	S	1(33)	0(0)	1(33)	2(67)	0(0)	0(0)	0(0)	0(0)	0(0)	2(67)	1(33)	-	-
	R	2(67)	3(100)	2(67)	1(33)	3(100)	3(100)	3(100)	3(100)	3(100)	1(33)	2(67)	-	-
***Citrobacter* spp(n=2**	S	0(0)	0(0)	0(0)	2(100)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	2(100)	-	-
	R	2(100)	2(100)	2(100)	0(0)	2(100)	2(100)	2(100)	2(100)	2(100)	2(100)	0(0)	-	-
***P.aeruginosa*(n=2)**	S	2(100)	-	2(100)	-	-	-	-	-	2(100)	2(100)	2(100)	2(100)	2(100)
	R	0(0)	-	0(0)	-	-	-	-	-	0(0)	0(0)	0(0)	0(0)	0(0)
***P.mirabilis* (n=1)**	S	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(100)	-	-
	R	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	1(100)	0(0)	-	-
***Serratia* spp(n=1)**	S	1(100)	1(100)	1(100)	1(100)	1(100)	0(0)	0(0)	1(100)	1(100)	1(100)	1(100)	-	-
	R	0(0)	0(0)	0	0(0)	0(0)	1(100)	1(100)	0(0)	0(0)	0(0)	0(0)	-	-
Total(n=18)	**S**	**11(61)**	**6(38)**	**11(61)**	**12(75)**	**8(50)**	**0(0)**	**0(0)**	**7(44)**	**10(63)**	**11(69)**	**14(88)**	**2(100)**	**2(100)**
	R	**7(39)**	**10(62)**	**7(39)**	**4(25)**	**8(50)**	**16(100)**	**16(100)**	**9(56)**	**6(37)**	**5(31)**	**2(12)**	**0(0)**	**0(0)**
Non-catheterized														
***E.coli* (n=10)**	S	8(80)	9(90)	8(80)	9(90)	6(60)	0(0)	0(0)	8(80)	9(90)	9(90)	9(90)	-	-
	R	2(20)	1(10)	2(20)	1(10)	4(40)	10(100)	10(100)	2(20)	1(10)	1(10)	1(10)	-	-
***K.pneumoniae* (n=2)**	S	2(100)	2(100)	2(100)	1(50)	1(50)	0(0)	0(0)	2(100)	2(100)	1(50)	2(100)	-	-
	R	0(0)	0(0)	0(0)	1(50)	1(50)	2(100)	2(100)	0(0)	0(0)	1(50)	0(0)	-	-
***Serratia* spp (n=2)**	S	1(50)	2(100)	1(50)	2(100)	1(50)	0(0)	0(0)	1(50)	2(100)	1(50)	2(100)	-	-
	R	1(50)	0(0)	1(50)	0(0)	1(50)	2(100)	2(100)	1(50)	0(0)	1(50)	0(0)	-	-
Total(n=14)	**S**	**11(79)**	**13(93)**	**11(79)**	**12(86)**	**8(51)**	**0(0)**	**0(0)**	**11(79)**	**13(93)**	**11(79)**	**13(93)**	-	-
	R	**3(21)**	**1(7)**	**3(21)**	**2(14)**	**6(49)**	**14(100)**	**14(100)**	**3(21)**	**1(7)**	**3(21)**	**1(7)**		

DST-Drug susceptibility pattern,CPR-ciprofloxacine,CTR-Ceftrixone,NOR-Norfloxacine,NIT-Nitrofurantoin,NAL-Nalidixic acid,AUG-Augumentine,AMP-Ampicilline,CXM-Cefexime,CFP-Cefepime,CN-Gentamicine,AKN-Amikacine,CAZ-Ceftazidime,PRL-Pipracilline

Table 7: Antimicrobial sensitivity pattern of Gram positive bacteria isolated from catheterized and non-catheterized UTI patients at University of Gondar Referral Hospital, February to May/2017.

Catheterized case	DSP	Antimicrobial agent number (%)									
		PEN	CN	TET	CXT	ERY	VAN	CPR	COT	NOR	NIT
S.aureus **(n=6)**	S	0(0)	2(33)	1(20)	2(33)	-	-	4(67)	0(0)	3(50)	6(100)
	R	6(100)	4(67)	5(80)	4(67)	-	-	2(33)	6(100)	3(50)	0(0)
CONS (n=5)	S	3(60)	1(20)	3(60)	0(0)	-	-	2(40)	1(20)	4(80)	5(100)
	R	2(40)	4(80)	2(40)	5(100)	-	-	3(60)	4(80)	1(20)	0(0)
Enterococcus **spp (n=2)**	S	1(50)	-	0(0)	-	0(0)	1(50)	0(0)	-	-	-
	R	1(50)	-	2(100	-	2(100)	1(50)	2(100)	-	-	-
Total (13)	S	4(31)	3(27)	4(31)	2(18)	0(0)	1(50)	6(46)	1(9)	7(64)	11(100)
	R	9(69)	8(73)	9(69)	9(82)	2(100)	1(50)	7(54)	10(91)	4(36)	0(0)
Non catheterized											
S.aureus **(n=3)**	S	2(67)	3(100)	1(33)	2(67)	-	-	3(100)	1(33)	3(100)	3(100)
	R	1(33)	0(0)	2(67)	1(33)	-	-	0(0)	2(67)	0(0)	0(0)
CONS (n=6)	S	4(67)	5(83)	3(50)	5(83)	-	-	3(50)	1(17)	4(67)	6(100)
	R	2(33)	1(17)	3(50)	1(17)	-	-	3(50)	5(83)	2(33)	0(0)
Entrococcus **spp (n=2)**	S	0(0)	-	0(0)	-	0(0)	1(50)	0	-	-	-
	R	2(100)	-	2(100)	-	2(100)	1(50)	2	-	-	-
Total (n=11)	S	6(55)	8(89)	4(36)	7(78)	0(0)	1(50)	6(56)	2(22)	7(78)	9(100)
	R	5(45)	1(11)	7(64)	2(22)	2(100)	1(50)	5(44)	7(78)	2(22)	0(0)

DST-Drug susceptibility pattern PEN-Pencillin,CN-Gentamicin,TET-tetracycline,CXT-Cefoxitine,ERY-Erythromicine,VAN-Vancomicine,CPR- Ciprofloxacine,COT-Cotrimoxazole,NOR-Norfloxacine,NIT-Nitrofurantoin,CONS-Coagulase negative staphylococcus specie

Table 8: Multi-drug resistant patterns in bacterial pathogens isolated from urine cultures among catheterized and non-catheterized patients attending the University of Gondar Referral Hospital, February to May/2017.

Anti-biogram patterns (%)								
Bacterial isolates	No (%)	R_0	R_1	R_2	R_3	R_4	$\geq R_5$	MDR
E.coli	12(21.4)	0	0	5(41.7)	4(33.3)	0	3(25.0)	7(58.3)
Klebsiella pneumoniae	9(16.0)	0	0	1(11.1)	4(44.4)	2(22.2)	2(22.2)	8(88.9)
Serratia spp	3(5.4)	0	0	1(33.3)	0	0	2(66.6)	2(66.7)
Citrobacter spp	2(3.6)	0	0	0	0	0	2(100)	2(100)
Enterobacter spp	3(5.4)	0	0	0	0	0	3(100)	3(100)
P.aeruginosa	2(3.6)	2(100)	0	0	0	0	0	0(0)
Proteus mirabilis	1(1.8)	0	0	0	0	0	1(100)	1(100)
CoNS	11(19.6)	1(9.1)	2(18.2	0	4(36.4)	0	4(36.4)	8(72.7)
S.aureus	9(16.0)	0	0	3(33.3)	2(22.2)	2(22.2)	2(22.2)	6(66.7)
Entrococcus spp	4(7.1)	0	0	0	2(50)	2(50)	0	4(100)
Total No (%)	56(100)	3(5.4)	2(3.6)	10(17.9)	13(23.2)	9(16.0)	19(33.9)	41(73.2)

Keys: $R_{0=}$ No antibiotic Resistance $R_{1=}$Resistant to one antibiotic class, R2=Resistant to two antibiotic class, R3= resistant to three antibiotic class, R4=Resistant to four antibiotic class, R5=Resistant to five and more than five antibiotic class, CoNS=Coagulase negative Staphylococci

5. DISCUSSION

Urinary tract infections (UTI) are likely to be more common in lower income countries than in the developed world (54). In the developed world with ready access to health care and antibiotic therapy, UTI tends to be cured very quickly Urinary tract infection attributed to the use of an indwelling urinary catheter is one of the most common infections acquired by patients in health care facilities (55).

In the present study the overall prevalence of UTI in both catheterized and non-catheterized patients was 25.5%. This finding was in agreement with the previous studies conducted in Addis Ababa 23% (45), Dessie 27.35% (46) and Bahirdar 30.2% (49). However, there was a report from Gondar (the same study area) with higher prevalence of UTI (52.8%) (56), while it was higher than reports from Jimma 9.2% (57) and Iran 8.06% (39). The differences in the prevalence of uropathogens might have been due to sample size variation, study design or the studies might have been based on retrospective survey and different environmental conditions and host factors, practices such as healthcare and education programmers, socioeconomic standards and hygiene practices in each geographical area.

Data of the present study also showed that the prevalence of UTI was higher among catheterized patients (41.4%) than non-catheterized patients (17.4%). These result also showed the presence of a statistically significant difference in the frequency of detection of UTI from non-catheterized and catheterized patients (17.4% versus 41.4%, $p<0.05$). This finding was concordant with the studies conducted in Jimma (43.3% vs22.2%) (45), and in Mekelle (39.5% vs12.5%) (47) for catheterized and noncatheterized patients, respectively. However, report from Saudi Arabia showed that the prevalence of community acquired and hospital acquired urinary tract infection was reported 55.3% and 44.7%, respectively (37). Different reports showed that catheter subverts several host defences and provides new binding sites for bacterial adhesins and its presence encourages the organism's persistent residence in the urinary tract (58). The risk factors that was significantly associated with that of CAUTI in the present study was the duration of the application of catheter (P=0.014). This data showed that patients catheterized for more than 2 weeks time had a UTI rate of 85.7%. Previous report from Nigeria documented that patients catheterized for more than 2 weeks had a UTI rate of 100% (59).

Catheter-associated urinary tract infection is the most common nosocomial infection in hospitals and nursing homes, comprising >40% of all institutionally acquired infections (10). Although sex was statistically insignificant, catheterized males had higher odds of UTI as compared to catheterized females. This might have been due to males have narrow urethra which may be damaged during catheterization as compared to females.

Among risk factors studied for non-catheterized UTI, sex was found to be important factor (P = 0.015). Females had a higher prevalence of UTI (25%) as compare to males (8.1%) in this study. There are also reports that documented higher prevalence of UTI among females compared with males in Saudi Arabia (78.7%vs21.3%) (37), Iran (88.7%vs11.3%) (39) and India (64.2%vs35.7%) (41). Women are more likely to develop UTIs than men. This is because, in women, the opening of the urethra is in close proximity to the anus and vagina, organisms can readily move from these openings to the urethra. The female urethra is also much shorter and wider than the male urethra, making it easier for bacteria to reach the bladder (14). Data of the present study showed no statistically significant association between age and UTI. However, UTIs are common in older adults. It is second only to respiratory infections in hospitalized patients and community-dwelling adults over the age of 65 years (60).

Another risk factor significantly associated with UTI in the present study was the presence of underlying disease (p=0.027). The odds of UTI in noncatheterized patients were higher in patients with underlying disease (35%) than who had no underlying disease (13%). This was consistent with previous studies of Debre tabor hospital, Ethiopia (10.9% and 4.7%) for diabetics and non diabetic patients respectively (61). The pathogenesis of UTI in patient with diabetes has been studied and the increased susceptibility is attributed to several impairments of host defence mechanisms such as leukocyte adherence, chemotaxis, and phagocytosis that can be impaired in diabetic patients (62). In addition, various impairments in the immune system, poor metabolic control, and incomplete bladder emptying due to autonomic neuropathy may all contribute to the enhanced risk of urinary tract infections in these patients (63).

At the time of diagnosis, catheterized patients with symptoms of dysuria and flank pain and non-catheterized patients with dysuria, suprapubic pain and tenderness were more likely to have culture confirmed UTI. This finding has significant value for physicians who are

working in resource limited countries where there is lack of microbiological culture in all health facilities. The term dysuria is used to describe painful urination, which often signifies an infection of the lower urinary tract. The discomfort is usually described by the patient as burning, stinging or itching. Pain occurring at the beginning of or during urination suggests a urethral site of disease, whereas pain after voiding implies pathology within the bladder or prostate area (64).

The present study showed that the etiologic pathogens of UTIs were mainly belongs to gram-negative bacteria 32 (57%) than Gram positive bacteria 24 (43%). This was in line with the previous studies conducted elsewhere (35, 43, 45). In this study, among catheterized patients, *Klebsiella pneumonia* was found to be the most frequently isolated pathogens which account 7(22.6%). This result was consistent with reports from Nigeria 26.6% (59). In contrast to reports from Jimma, *Staphylococcus aureus* was found to be the second most frequent pathogen accounts 19.4%. On the other hand, among the noncatheterized patients, *E.coli* was the most frequently isolated bacteria which was (40%) and Coagulase negative staphylococcus species was the second most frequent pathogen accounts (24%). This result also agrees with previous report from Jimma (45).

In this study, isolates of *Pseudomonas aeruginosa, Proteus mirabilis, Citrobacter* spp. and *Entrococcus* spp. were found exclusively among catheterized patients. There are reports that showed UTI caused by many of the aforementioned bacteria could possibly be nosocomial origin. Particularly, UTI caused by *Pseudomonas* species and *Proteus* species are associated with hospital acquired infections often following catheterization (31, 52).

Gram-negative isolates from both groups of patients (non-catheterized vs. catheterized) showed a high level (100%) of resistance to ampicillin and augmentin. This result showed high resistance rate than the previous studies in the same area 95.2% (56) and Bahirdar 80% (50). This change of resistance pattern might be due to self-medication and indiscriminate use of antibiotics in the study area. On the other hand high level of sensitivity were detected to antibiotics such as amikacin, ceftriaxone, ciprofloxacin, norfloxacin, nitrofurantoin, nalidixic acid, gentamicin, cefepime, cefexime and a comparable rate of sensitivity has been reported for these drugs in the previous studies in India (41) and Debretabor (61). Low resistance was observed for these drugs because they are not easily accessible and relatively

expensive in price compared to others. Thus, these drugs could be considered as alternative options in the empirical treatment of UTIs. Similarly, in this present study, a higher proportion of isolates of gram positive bacteria were in average resistant to cotrimoxazole (84.5%), tetracycline (66.5%), penicillin (58.3%), and ciprofloxacin (49%). This result was also consistent with report from Debretabor (61). In this study, methicillin resistant *S.aureus* was detected in 55.6% of cases. It was lower than reports from India (66.6%) (41).

Bacterial pathogens isolated from catheterized patients showed high resistance rate than noncatheterized ones. The *E.coli* isolates from catheterized patients exhibited resistance to ciprofloxacin, norfloxacin, nalidixic acid, cefepime and cefexime(50%) for each, whereas *E.coli* from noncatheterized patients were less resistant to the above mentioned antibiotic disks.

In addition to these, CoNS isolated from catheterized patients showed more resistant to cefoxitine, gentamycin and ciprofloxacin than noncatheterized patient isolate. Whereas, *S.aureus* isolate from catheterized patients also showed resistance to penicillin, cotrimoxazole, tetracycline, gentamycin and cefoxitine than noncatheterized patients. *Entrococcus* species from catheterized patients also exhibited (100%) resistance to ciprofloxacin than noncatheterized ones. This result is consistent with previous report from Jimma (45) and Bahirdar (50).This change of resistance between catheterized and noncatheterized bacterial isolate might be because of all isolates from catheterized patients were of nosocomial origin, the wide use of antimicrobial agents in the hospital setting may contribute for the particular resistance pattern of catheter urine isolates or bacterial isolates in catheterized patients might be going to biofilm formation covered by strong polymicrobial structure which leads the bacteria resistant to many antimicrobials.

In this study multidrug resistance to three or more antimicrobial classes was observed in 73.2% of the isolates. This was consistent with the previous report from Bangladish 70.67% (65) and lower than the previous report from Bahirdar 93.1% (50) and Gondar 86.5% (56). The lower multidrug resistance rate of isolates in this study could be due to rational use of antimicrobial agents or the present study used a recent guideline about the definition of MDR allowed to decrease from the previous reports.

6. LIMITATIONS OF THE STUDY

This study had limitations including being hospital based study where asymptomatic cases of UTI might have been missed further limiting its generalizability to the whole population. It also involved a small sample size especially for antimicrobial susceptibility testing which limits the recommendations for revising treatment guidelines. Moreover, due to lack of facility and budget isolation of other etiologic agents including anaerobic bacteria, bacteria unable to grow on culture, parasites, fungi and virus were not done.

7. CONCLUSION

One fourth of clinically suspected UTI patients had culture confirmed UTI. Catheterized patients for more than two weeks and non-catheterized females and patients with chronic diseases had higher isolation rates of bacterial pathogens as compared to their counter parts. The predominant bacterial isolates were *E.coli* followed by Coagulase negative *staphylococcus* species, *K. pneumoniae and S. aureus*. Isolation of *E.coli* was significantly associated with non catheterized patients. Amikacin, nitrofurantoin, norfloxacin, ciprofloxacin and ceftriaxone were the drug of choice for gram negative isolates whereas nitrofurantoin, norfloxacin and gentamicin were for most gram positive bacteria.

Alarmingly high rate of MDR to commonly used antimicrobials from UTIs were reported. Particularly, increasing resistance in pathogens isolated from catheterized patients is frustrating.

8. RECOMMENDATIONS

Based on this study the following recommendations are made:

- Physicians working in a hospital should follow strict aseptic technique during indwelling catheter insertion and minimize the duration and unnecessary use to reduce the risk of CAUTIs.
- Catheterized patients for more than 2 weeks should be screened for UTI using culture and treated based on antibiotic sensitivity test rather than empirical treatment.
- Medical Microbiologists in the hospital integrated with the academic staff should conduct continuous surveillance to check the pattern of common bacterial isolate and antibiotic resistance including MDR.
- Researchers should conduct a robust study with large number in multisite inform policy makers and concerned bodies to change a guideline.
- The hospital administration has to strengthen the existing antimicrobial stewardship committee to reduce emergence of antimicrobial resistance.

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ANNEXES

Annex I: Information sheet and consent form

Study Title: Assessment of bacterial pathogens, antimicrobial susceptibility pattern and associated risk factors among catheterized UTI suspected patients compared with non catheterized ones at University of Gondar referral hospital, Northwest Ethiopia.

Name of the Sponsor: Amhara Regional Health Bureau.

Name of the Organization: School of Biomedical and Laboratory Sciences, Gondar College of Medicine and Health Sciences, University of Gondar.

1. Purpose of the Research Project: The aim of this study is to assess the Bacterial Pathogens, their antimicrobial Susceptibility Pattern and associated risk factors among catheterized UTI suspected patients compared with non-catheterized ones attending University of Gondar referral hospital, Gondar, North West Ethiopia. In line with this the findings will also provide baseline information for health sector administrators, concerned bodies and the patients themselves in planning and managing of UTIs that further reduce the morbidity and mortality associated with the disease.

2. Procedure: In order to perform the above mentioned study at University of Gondar referral hospital, you are invited to take part in this project. If you are willing to participate, you need to understand the purpose of the study and give your consent **.**The required clinical sample will be collected by nurses and who are currently working inpatient and outpatient department of the hospital. Then, you will be requested to give your consent to the sample collector. Socio-demographic, associated factors and clinical information will be collected from the study participants using pre tested structured questionnaires via interview technique; since you fulfil the criteria you are kindly requested to give the required urine sample and genuine answers to the prepared questionnaire.

3. Risk associated with the study: You will not be at any physical or psychological risk and no damage resulting from the research procedures.

4. Benefits of the study: Based on the diagnosis result you will be treated accordingly. Moreover, this study will have a great value on preventive measures in hospitals and in the community. The results of this study have importance to treat the patients and to use as a baseline for effective treatment in the absences of laboratory investigation

5. Compensation for participation: You will not receive any payment for your participation in this research study.

6. Confidentiality of your information- All information gathered from the study participant will remain confidential. Your participation in this study is strictly anonymous. Personal information will be treated confidentially and under no circumstances it will not be transmitted to any person or organization. The results of this study will be evaluated and summarized, and a feedback of the results to the study participants will be given by principal investigator.

7. Right to Refusal or Withdraw: Your participation in the study is absolutely voluntary; you have full right to refuse from participating in this research. You can refuse to give sample and not to respond any or all the questionnaires and this will not affect you on using any kind of services from the hospital.

8. Person to Contacts: This research project will be reviewed and approved by Ethical clearance committee of School of Biomedical and laboratory Sciences, College of Medicine and Health Sciences, University of Gondar. If you want to know more information, you can contact the following individuals and you may ask at any time as you want:-

1-School of Biomedical and Laboratory Sciences, UOG
P.Box-196, Gondar, Ethiopia
2. Mr.Wudu Tafere, principal investigator
Mobile: +251918072587/ e-mail: taferewudu@gmail.com
3. Dr Baye Gelaw, (advisor), University of Gondar
Mobile: 0918 703723 /e-mail: tedybayegelaw@gmail.com
4. Mr.Teklay G.cherkos, (advisor), University of Gondar
Mobile: 0922795314 /e-mail estiftg17@gmail.com

Consent form

Serial No----------Name of health institution----------Card No----------Date----------

I the undersigned study participant with urinary tract infection have been well informed about the objective of the study entitled "Assessment of Bacterial Pathogens and their Antimicrobial Susceptibility Pattern among UTI patients with history of Catheter compared with non-Catheterized ones attending Gondar referral hospital, North West Ethiopia, February to May 2017.

I am also informed that all the information obtained at any course of the study is to be kept confidential. Moreover, I have also been well informed of my right to keep hold of, decline to cooperate and drop out of the study if I want and none of my actions will have any bearing at all on my overall health care and hospital access.

I agreed voluntarily to provide the requested samples from me as well as my child.

Name and signature of study participant _____ Date_____

Name and signature of investigator _____ Date_____

Assent form for child

I have read and/or listened to the description of the study and I understand what the procedures are and what will happen to me in the study. I have received permission from my parent(s)/guardian(s) to participate in the study and I agree to participate in it. I know that I can quit the study any time.

_____ _____

Signature of Child /guardians Date

_____ _____

Signature of Investigator Date

Annex II: Amharic Version Study Participant Information and Consent Form

የመረጃና የስምምነት ዉል ቅጽ

የጥናቱ ርእስ -የሽንት ቧንቧ ህመምን የሚያመጡ የባክተሪያ ዝርያዎችን ካቲተር በሚጠቀሙና በማይጠቀሙ በሽተኞቸ ላይ መለየትና ለጸረ-ባክቴሪያ መድሃኒት ያላቸውን ሁኔታ ለማወቅ በጎንደር ሪፈራል ሆስፒታል በሚታከሙ ሕመምተኞች ሽንት ውስጥ መኖራቸውን መለየት

የጥናቱ ደጋፊ - የአማራ ብሔራዊ ክልላዊ መንግስት ጤና ቢሮ፡፡

የድርጅቱ ስም ጎንደር ዩኒቨርሲቲ ህክምና ና ጤና ሳይንስ ኮሌጅ የላቦራቶሪ እና ባዮሜዲካል ትምህርት ቤት

1. የጥናቱ ዓላማ- የዚህ ጥናት አላማ የሽንት ቧንቧ ህመምን የሚያመጡ የባክተሪያ ዝርያዎችን ካቲተር በሚጠቀሙና በማይጠቀሙ በሽተኞቸ ላይ መለየትና ለጸረ-ባክቴሪያ መድሃኒት ያላቸውን ሁኔታ ለማወቅ በጎንደር ሪፈራል ሆስፒታል በሚታከሙ ህመምተኞች ሽንት ውስጥ መኖራቸውን መለየትና ማሳወቅ ነው፡፡አያይዞም ከጥናቱ የሚገኘው ውጤት ለጤና ተቋም አስተዳዳሪዎች ለሚመለከታቸው አካላት እና ለሕሙማን ለራሳቸው በዚህ ጀርም የሚከሰተውን ሕመምና ሞት ለመከላከል መሠረታዊ መረጃዎችን ይሰጣል፡፡
2. የአሰራር ሂድት- ይህን ጥናት በጎንደር ሪፈራል ሆስፒታል ለመስራት የጥናቱ ተሳታፊ እንዲሆኑ ተጋበዘዋል፡፡ ለመሳተፍ ፍቃደኛ ከሆኑ የጥናቱን ዓላማ መረዳትና ፍቃደኝነትዎን መግለፅ ይጠበቃል፡፡ለዚህ ጥናት የሚያስፈልገው የቁስል ናሙና የሚሰበሰበው በጥናቱ ወቅት በተመላላሽና ተኝቶ ታካሚ ክፍል ዉስጥ በሚሰሩ ነርሶች ይሆናል፡፡እንዲሁም በተጨማሪ ማህበራዊ ነክ ኢጋላጭ ሁኔታዎች እና የጤንነት ሁኔታን የሚያሳዩ ጥያቀዎች ከያንዳንዱ የጥናቱ ተሳታፊዎች በመጠይቁ መሰረት ይሰበሰባል፡፡እርስዎም መስፈርቱን እስካሟሉ ድረስ የሚያስፈልገዉን ናሙና ለመስጠት እና ለተዘጋጀው ጥያቄ ትክክለኛ ምላሽ እንዲሰጡ በትህትና ይጠየቃሉ፡፡
3. ከጥናቱ ጋር ተያይዞ የሚመጣ ጉዳት - በዚህ ጥናት ዝርዝር ላሰራር ሂደት ውስጥ አካላዊ ወይም አእምሮአዊ ጉዳት አይኖርም፡፡
4. ጥቅሞች - በምርመራ ውጤትዎ መሠረት ሕክምና ያገኛሉ በተጨማሪም ይህ ጥናት የመከላለል ስራ በሆስፒታል እና በህብረተሰቡ ዘንድ እንዲኖር ያግዛል፡፡ እንደዚሁም ደግሞ የላቦራቶሪ አገልግሎት በሌለበት ጤና ተቋም ትክክለኛ መድሃኒት ለመስጠት እንደ አመላካች ሆኖ ያገለግላል፡፡
5. ለተሳትፎ የሚሰጥ ማካካሻ- ምንም አይነት የካሳ ክፍያ የለዉም
6. የጥናቱ መረጃ ሚስጥራዊነት ሁሉም ከተሳታፊዎች የሚሰበሰቡ መረጃዎች በሚስጢር የሚያዙ እና የሚጠበቁ ይሆናሉ፡፡ በማንኛውም ምክንያት ተሳታፊዎች እነማን መሆናቸውን የሚያሳይ በመጠይቁ ይሁን በሌላ ነገር አይኖርም፡፡ የተሰበሰቡ መረጃዎች ለሶስተኛ ወገን ተላልፎ አይሰጥም፡፡ በተጨማሪም ውጤቱ የሚለካዉ ይሁን ተሰብስቦ የሚያዘው በዋና አጥኚ ነው፡፡

7. የመዉጣት (የማቋረጥ) መብት - በዚህ ጥናት ላይ መሳተፍዎ በሙሉ ፍቃደኝነት ላይ የተመሰረተ ነው ::ጥናቱን የማቋረጥ ሙሉ መብት አለዎት ። ናሙናም ሆነ ለመጠይቁ መልስ ያለመስጠት ከሆስፒታሉ የሚያገኙትን ማነኛውንም አገልግሎት አይገድብም ።
8. የሚያገኙዋቸው ሰዎች- ይህ ጥናት በጎንደር ዩኒቨርሲቲ የስነምግባር ምርምር ኮሚቴና ሕክምናና ጤናሳይነንስ ኮሌጅ የላቦራቶሪ ባዮሜዲካል ትምህርት ክፍል ተዕልኮ የሚጸድቅ ይሆናል። ጥያቄ ካለዎት ተጨማሪ መረጃ ከፈለጉ በማንኛዉም ጊዜ ከዚህ በታች የተጠቀሰዉን አድራሻ መጠቀም ይችላሉ።

1. ባዮ ሜዲካል እና ላቦራቶሪ ሳይንስ።
   ፖ.ሳ ቁ-196, ጎንደር ኢትዮጵያ
2. አቶ ውዱ ታፈረ፣ ዋና ተመራማሪ:
   ስ.ቁ: +251918072587 ኢ.ሜል taferewudu@gmail.com
3. ዶ/ር ባዬ ገላው: አማካሪ ጎንደር ዩንቨርሲቲ
   ስ.ቁ:0918703723--ኢ.ሜል tedybayegelaw@gmail.com
4. አቶ ተክላይ ገ/ጨርቆስ - አማካሪ ጎንደር ዩንቨርሲቲ
   ስ.ቁ:-0922795314 ኢ.ሜል estiftg17@gmail.com

የስምምነት ውል

የአዋቂዎች የስምምነት ማረጋገጫ ፊርማ

ተራ ቁጥር----------የሚታከምበት ጤና ተቋም----------የካርድ ቁጥር----------

ቀን----------

እኔ ከዚህ በታች ስሜ የተጠቀሰዉና የፊረምኩት የጥናቱ ተሳታፊ የሸንት ቧንቧ ህመምን የሚያመጡ የባክተሪያ ዝርያዎችን የሸንት ማሸኛ ቱቦ በሚጠቀሙና በማይጠቀሙ በሽተኞች ላይ መለየትና ለጸረ-ባክቴሪያ መድሃኒት ያላቸውን ሁኔታ በጎንደር ሪፈራል ሆስፒታል በሚታከሙ ህመምተኞች ሸንት ውስጥ መኖራቸውን ለመለየት እና ለማሳወቅ የሚደረገውን ጥናት አላማና ጥቅም በሚገባ ተረድቻለሁ፡፡ ጥናቱ ላይ መሳተፍም ሆነ አለመሳተፍ በራሴ ፍቃድ የሚወሰን መሆኑም ተገልጾልኛል፡፡ በተጨማሪም ከጥናቱ ባልሳተፍም ሆነ አቋርጬ ብወጣ ከሆስፒታሉ በማገኘዉ የህክምና አገልግሎት ምንም አይነት ችግር እንደማይደርስብኝ ተነግሮኛል፡፡

በመሆኑም ከእኔም ሆነ ከልጄ ሸንት ናሙና መዉሰድ አስፈላጊ መሆኑን ስለተስማማሁበት ለመስጠት ሙሉ ፈቃደኛ መሆኔን በፊርማዬ እገልጻለሁ፡፡

የተሳታፊ ፊርማ _____ ቀን _____

የተመራማሪ ስምና ፊርማ _____ ቀን _____

የልጆች የስምምነት ማረጋገጫ ፊርማ

እኔ የጥናቱ ተሳታፊ የጥናቱን ሂደት እና በጥናቱ ጊዜ ስለሚያጋጥሙኝ ነገሮች በሚገባ የተረዳሁ ና በጥናቱ ለመሳተፍ ከአሳዳጊዎቼ/ ከቤተሰቦቸ ፍቃድ አግንቻለሁ፡፡ ከጥናቱ በማንኛዉም ደረጃ እራሴን ማግለል እንደምችል ተረድቻለሁ እናም በጥናቱ ለመሳተፍ ተስማምቻለሁ፡፡

የተሳታፊዉ ልጅ /አሳዳጊ ፊርማ----------ቀን----------

የዋና ተመራማሪ ፊርማ----------ቀን----------

Annex III: English Version Questionnaire

Questionnaire for assessment of sociodemographic, clinical profile and laboratory data of UTI Patients at University of Gondar referral Hospital, North West, Ethiopia.

Questionnaire code #	
Card #	
Date of data collection	
Name of health institution	

I. Socio demographic information

101. Age ……

102. Sex 1.Male 2.Female

103. Residence 1.Urban 2.Rural

104. Occupation 1. Civil servant 2.Farmer 3.Merchant 4.House wife
5. Self employer 6. Other specify.....

105. Educational status 1.Unable to write &read 2.Read &write only 3.primary
4. Secondary 5.University/college

106. Marital status 1.Married 2.Single 3.Divorced 4.Widowed

107. Patient setting 1.Outpatient 2.Inpatient

108. If being inpatient, how many days do you stay? .....

109. Ward: Medical _____
Surgical _____
Gyn & ObS _____
Pediatrics _____
Others _____

II. Associated risk factors:

201. Catheterized Patients 1.Yes 2.No

202. If yes, for how long: 3 days 1 week 2 weeks >2 weeks

203. Reason for catheterization…….

204. If say no; are you pregnant (for female) 1. Yes 2. No

For both catheterized and non-catheterized UTI patient:

205. History of previous catheterization: 1.Yes 2.No

206. If yes, state reason for previous catheterization……..

207. Did you have past history of UTI with in 1 year 1.Yes 2.No

208. If yes how many times? ……....

209. History of previous antibiotic treatment 1.Yes 2.No

210. Is there any other underlying disease: 1.Yes 2.No

211. If yes, specify the type of disease……

III. Clinical Profile

	YES	NO
301. Fever	____	____
302. Dysuria	____	____
303. Urgency	____	____
304. Frequency	____	____
305. Flank pain	____	____
306. Suprapubic pain	____	____
307. Others specify:	____	____

IV. Laboratory Data

401. Date of urine collection----------

402. Type of specimen: Catheter urine sample……

Mid stream urine sample……..

403. Cultures and Identification

Significant bacteriuria: Yes_____

No_____

Name of the bacteria isolated_____

404. Antimicrobial susceptibility testing	S	I	R
1. Amikacin	-----	------	------
2. Ampicillin	-----	-----	------
3. Amoxicillin-clavulanic acid	------	------	------
4. Ceftriaxone	------	------	------
5. Ciprofloxacin	------	------	------
8. Nitrofurantoin	------	-------	-------
9. Cotrimoxazole	------	--------	--------
10.Nalidixic acid	-------	--------	--------
11.Cefepime	------	-------	-------
12.Cefixime	------	-------	-------
13. Penicillin	-------	--------	--------
14.Erythromicine	-------	--------	-------
15. Tetracycline	-------	--------	-------
16. Vancomycine	-------	-------	-------
17.Gentamycine	------	-------	-------
18.Cefoxitine	-------	--------	-------

V. Comments_____

Annex IV: Amharic Version of Questionnaire

የአማርኛ መጠይቅ

የጥናቱ ርእስ፡- የሸንት ቧንቧ ህመምን የሚያመጡ የባክተሪያ ዝርያዎችን ካቲተር በሚጠቀሙና በማይጠቀሙ በሽተኞች ላይ መለየትና ለጸረ
ባክቴሪያ መድሃኒት ያላቸውን ሁኔታ ለማወቅ በሳንደር ሪፈራል ሆስፒታል በሚታከሙ ሕመምተኞች ሽንት ውስጥ መኖራቸውን መለየት

የኮድ ቁጥር	
የመታከሚያ ካርድ ቁጥር	
ናሙናዉ የተወሰደበተ ቀን	
የጤና ተቋሙ ስም	

ሀ. ማህበራዊ ና ኢኮኖማዊ መረጃ

101	እድሜ ?	----------
102	ጸታ	1.ወንድ 2.ሴት
103	የትምህርት ደረጃ	**1.** ያልተማረ 2.ማንበብ እና መጻፍ 2.የመጀመሪያ ሳይክል 3. የሁለተኛ ሳይክል 4. የከፍተኛ ትምህርት
104	መኖሪያ ቦታ	1.ገጠር 2. ከተማ
105	ስራ	1.የመንግስትሰራተኛ 3. ነጋዴ 2.ገበሬ 4. የቤትእመቤት 5.የቀን ስራ 6.ሌላ ከሆነ ይግለጹ--------
106	የታካሚዉ ሁኔታ	1.ተኝቶ ታካሚ (ለስንት ቀን ተኙ.....) 2.ተመላላሽ ታካሚ

107	በሽተኛው የተኛበት/ችበት ክፍል	1.ሜዲካል 3.ማዋለጃ ክፍል 2.ቀዶጥገና ክፍል 4.ህፃናት ክፍል 5.ሌላ ክፍል...
108	የጋብቻ ሁኔታ	1.ያገባ/ች 2.ያላገባ/ች 3.የፈታ/ች 4.በግልሙትና የሚኖር/የምትኖር

ለ .ለሽንት ቧንቧ ህመም መባባስ አጋላጭ ሁኔታዎች

ጥያቄ ቁጥር	ጥያቄ	መለያ
201	የሽንት ማሸኛ ቱቦ ተጠቃሚ ነዎት?	**1.** አዎ 2. አይደለሁም
202	መልስዎ አዎ ከሆነ ምንያህል ጊዜ ሆነዎት?	1. 3 ቀን 3. 2 ሳምንት 2. 1 ሳምንት 4. ከ2 ሳምንት በላይ
203	የሽንት ማሸኛ ቱቦ እንዲጠቀሙ የተደረገበት ምክንያት?	.....
204	ነፍሰጡር ነዎት?	1.አዎ 2.አይደለሁም
	የሽንት ማሸኛ ቱቦ ለሚጠቀሙም ለማይጠቀሙም የሚጠየቅ	
205	ከዚህ በፊት የሽንት ማሸኛ ቱቦ ተጠቅመው ያውቃሉ?	1. አዎ 2. የለም
206	አዎ ከሆነ በምን ምክንያት?	.....
207	በ ነ አመት ጊዜ ውሰጥ የሽንት ቧንቧ ህመም አሞዎት ያውቅ ነበር?	1. አዎ (ስንት ጊዜ.....) 2. የለም
208	መልስዎ አዎ ከሆነ መድሃኒት ወስደው ነበር?	1. አዎ (ምን አይነት)..... 2. የለም
209	ሌላ ስር የሰደደ የቆየ ህመም አለዎት?	1.አዎ (ይገለፅ.....) 2.የለም

ሐ. የሽንት ቧንቧ ህመምን አመላካች ምልክቶች

ጥያቄ ቁጥር	ምልክቶች	አዎ	የለም
301	የሰውነት ሙቀት መጨመር(ትኩሳት)		
302	ሽንት በሚሸኑበት ጊዜ የሚቃጠል ስሜት		
303	ሽንትን መቆጣጠር አለመቻል		
304	ቶሎ ቶሎ የመሸናት ሁኔታ		
305	የሽንጥ/ወገብ ህመም ስሜት		
306	ከሆድ በታች ያለ የህመም ስሜት		
307	ሌላ ካለ ይገለጽ.....		

አመሰግናለሁ!!!

Annex V: Procedures

A. Culture media preparation

1. Read the label on a bottle of dehydrated agar media. It specifies the amount of dehydrated powder required to make 1 litter (1,000 ml) of medium. Calculate the amount needed for 1/2 litter and weigh out this quantity.
2. Place 500 ml of distilled water in an Erlenmeyer flask. Add the weighed, dehydrated agar while stirring with a glass rod to prevent lumping.
3. Set the flask on a tripod over an asbestos mat.
4. When the agar mixture is completely dissolved, remove the flask from the flame or hot plate, close it with the cotton plug or cap, and it has to be sterilized in the autoclave.
5. When the flask of sterilized agar is returned to you, allow it to cool to about 50°C (the agar should be warm and melted, but not too hot to handle in its flask). Remove the plug or cap with the little finger of your right hand and continue to hold it until you are sure it won't have to be returned to the flask. Quickly pour the melted, sterile agar into a series of petri dishes. The petri dish tops are lifted with the left hand and the bottoms are filled to about one-third capacity with melted agar.
6. Replace each petri dish top as the plate is poured. When the plates are cool (agar solidified), invert them to prevent condensing moisture from accumulating on the agar surfaces.
7. Place inverted agar plates in the 35°C incubator. They should be incubated for at least 24 hours to ensure their sterility (free of contaminating bacteria) before we use.

B. Collection and processing of urine specimen

The specimen (mid-stream and catheterized urine) will be collected by an experienced nurse and special care should be taken to avoid contaminating the specimen with commensal organisms from the vagina and skin.

1. With sterile wide mouth urine cup collect urine sample from UTI patients.
2. Label the sample as soon as possible with the patient code number
3. Inoculate in to CLED, MacConkey and blood agar aseptically
4. Incubate the plate aerobically at 35-37 °C for 18-24 hours.
5. Examine and report the culture; look for colony characteristics and perform biochemical test.
6. Determine drug susceptibility pattern of the isolated organism

C. Gram stain procedures

1. Prepare a thin smear of the culture or specimen will be observed.
2. Allow to air-dry and fix the smear.
3. Cover the fixed smear with crystal violet for 1 min.
4. Rinse with clean water and tip off all the water.
5. Cover the smear with Lugol's iodine for 1 min.
6. Wash off the iodine with clean water.
7. Add acetone-alcohol for 30 sec.
8. Wash the smear immediately with clean water.
9. Cover the smear with saffranin for 1-2 minutes.
10. Rinse with clean water.
11. Wipe the back of the slide and place in a draining rack for the smear to air-dry.
12. Examine microscopically, first with the 40x objective and then with the oil immersion objective for white cells, bacteria and other structures.

13. Result interpretation

- Gram- positive bacteria ----------Dark purple

- Gram- negative bacteria ----------Pale to dark red.

D. Biochemical testing procedures

Identification of Gram positive bacteria: Gram-positive cocci will be identified based on their Gram reaction, catalase and coagulase test results.

Catalase test: This test will be used to differentiate *staphylococci* (+ve) from *streptococci (*-ve)

Procedure

1. Pour 2-3 ml of 3% hydrogen peroxide to a test tube
2. Using a sterile wooden stick take the test organism and immerse into the hydrogen peroxide solution
3. Look for immediate bubbling
4. Interpretation :Active bubbling--positive test and No release of bubbles-negative test

Coagulase test: This test is used to differentiate *S. aureus* from other *Staphylococcus* spp

Procedure

1. Place a drop of physiological saline on two separate slides
2. Emulsify the test organism in each of the drop to make thick suspension
3. Add one drop of plasma to one of the suspensions and mix gently. Look for clumping of the organism within 10 seconds
4. Interpretation

   Clumping within 10 seconds ----------*S.aureus*

   No clumping within 10 seconds ----------other staphylococcus species

Identification of Gram negative bacteria: was based on their test result with a series of biochemical tests.

Procedure

1. Prepare a suspension of the test organism with nutrient broth. 3-4 colony of test organism in 5 ml nutrient broth.
2. A loop full of the bacterial suspension is inoculated in to indole, citrate agar, triple sugar iron agar, lysine decarboxylase agar, Mannitol, urea agar and motility medium.
3. Incubate at 35-37 ^{O}C for 18-24 hours.

4. Look for colour change (turbidity for motility) of the medium
5. Identify the test organism by considering the result of the six biochemical tests

E. Antimicrobial susceptibility testing

Procedure

1. Prepare a suspension of the test organism by emulsifying several colony of the organism in a small volume of nutrient broth.
2. Much the turbidity of suspension with turbidity standard
3. With a sterile swab take sample from the suspension (squeeze the swab against the side of the test tube to remove the excess fluid).
4. Spread the inoculums evenly over the Muller-Hinton agar plate with the swab
5. Using a sterile forceps or needle, place the antimicrobial disc on the inoculated plate
6. Incubate the plate aerobically at 35-37^{o}C for 18-24 hours.
7. Read the test after checking that the bacterial growth is neither heavy nor light. Measure the radius of the inhibition zone.
8. Interpret the reaction of the test organism to each antibiotics used as sensitive, intermediate, or resistance as per the standard Sensitive – zone of radius is wider or equal to the control.

DECLARATION

The research work in this thesis entitled **"Assessment of bacterial pathogens, antimicrobial susceptibility pattern and associated risk factors among catheterized UTI suspected patients compared with non-catheterized patients at University of Gondar Referral Hospital, Northwest Ethiopia."** was carried out by me under the supervision of Dr Baye Gelaw and Mr Teklay G/cherkos at the University of Gondar, College of Medicine and Health Sciences, School of Biomedical and Laboratory Sciences, Department of Medical Microbiology, for the award of MSc Degree in Medical Microbiology. I declare that this work is original and has not been submitted to any other University or institution.

Name of student's: Wudu Tafere

Tel: 0918072587 *Email:taferewudu@gmail.com.*

Place: Gondar, 2017 Sign: _____ Date: _____

Advisors	Sign	Date
1. Dr.Baye Gelaw	_____	_____
2. Mr. Teklay G/cherkos	_____	_____
Examiners	Sign	Date
1._____	_____	_____
2._____	_____	_____